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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/502,470

12/03/2004

Aylwin Ng

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EXAMINER

YAO, LEI

ART UNIT

PAPER NUMBER

1642

MAIL DATE

DELIVERY MODE

06/20/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/502,470	<b>Applicant(s)</b> NG ET AL.	
	<b>Examiner</b> LEI YAO	<b>Art Unit</b> 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 18 March 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 31-34 and 43-45 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 31-34, 43-45 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

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### ***Response to Arguments***

The Amendment filed on 3/18/2008 in response to the previous Non-Final Office Action (10/9/2007) is acknowledged and has been entered.

Claims 1-30 and 35-42 are cancelled.

Claims 31-34 and 43-45 are pending and are under consideration for a method of treating nasopharyngeal cancer (NPC) comprising administering a demethylation agent combined with a chemo or radiotherapy.

The following office action contains NEW GROUNDS of rejection based on new consideration.

### ***Specification and Sequence***

It is acknowledged that the specification has been amended to delete hyperlink and add SEQ ID NO to the sequence in response to the last Office action.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1996), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103 (a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or obviousness

Claims 31-33 and 43-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kuratomi et al., (Eur Arch Otorhinolaryngol, vol 256, page S60-63, 1999, provided in the Office action

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dated 10/9/2007) in view of Lo et al., (Cancer Research. Vol 61, page 3877-3881, 2001) and Momparler et al., (anticancer Drugs, vol 8, page 358-6, 1997, provided in the Office action dated 10/9/2007) as evidenced by Kwong et al., (Clin Cancer Res vol 8 page 131-137, Jan 2002).

Claims are drawn to a method of treating an individual with a nasopharyngeal cancer (NPC) comprising administering to said individual a demethylation agent in association with a second cancer treatment (claim 31), wherein second cancer treatment is chemo- or radio-therapy (claim 32), wherein the demethylation agent is 5-aza-2-deoxycytidine (claim 33, 43), wherein NPC is type I (claims 44 and 45).

The specification teaches that the type of NPC is defined based on WHO classification, in which type I NPC is differentiated squamous cell carcinoma with cellular keratin [0003].

Kuratomi et al., teach a method of treating a NPC patient by administering a chemotherapeutic drug (e.g. 5-fluorouracil) combined with radiotherapy (entire reference). Kuratomi et al., also teach that the NPC patients comprising undifferentiated, poorly differentiated, and moderately differentiated squamous cell carcinoma (SSC) respond to the treatment differently, in which undifferentiated carcinoma (type II or III) respond better than more differentiated SSC (page 60 and 61 figure 1).

Kuratomi et al., do not teach a demethylation drug comprising 5-aza-2-deoxycytidine as an chemotherapeutic drug in the treatment of NPC patient.

It is well known in the art that gene expression could be inactivated by methylation of the promoter region. High frequency of the methylation in the promoter region of the tumor suppressor genes in the NPC cells has been reported. For example, Lo et al., teach promoter hypermethylation of the RASSF1A gene expressed in the nasopharyngeal carcinoma cells and not in the normal nasopharyngeal cells (entire reference). Lo et al., teach that demethylation is detected in the cells treated with demethylation agent, 5'-Aza-2'-deoxycytidine (page 3878, col 1 and page 3880, col 2). Hypermethylation of multiple tumor suppressor genes in the nasopharyngeal carcinoma cells and primary tumors are also evidenced by Kwong et al., (abstract and entirety of the reference).

Momparler et al., also teach that 5-aza-2'-deoxycytidine is an analog of deoxycytidine to block the DNA methylation and has been experimentally used as anti-cancer agent for cancers (page 358).

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Momparler et al., then teach a method of treating the patients with lung squamous cell carcinoma by administering the patient with the 5-aza-2-deoxycytidine (page 361-362, table 1 and figure 1).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the teachings to treat NPC comprising administering a demethylation agent 5-aza-2' deoxycytidine with expected result. One of ordinary skill in the art at the time the invention was made would have been motivated to apply the teaching of Lo and evidence by Kwong to the teachings of Kuratomi and Momparler in order to advance the treatment for NPC patients with combined anticancer treatment comprising 5-aza-2-deoxycytidine because Kuratomi et al., suggest that NPC patient is highly responsive to combined therapy (page s60, col 2) and Lo and Kwong have suggested hypermethylation of tumor supressor genes in the NPC, not in the normal nasopharyngeal cells. One of ordinary skill in the art at the time the invention was made would have been motivated with reasonable expectation of sucess to treat type I NPC (differentiated squamous cell carcinoma) patient comprising administering the demethylation drug 5-aza-2-deoxycytidine because Momparler et al have suggested that karatin positive squamous cell carcinoma cell is sensitive to the drug and Kuratomi et al., teach that the currently used chemotherapeutic agents and/or radiation has less effective to the moderately differentiated squamous cell carcinoma (type I is defferentiated squamous cell carcinoma, page S61, figure 1). One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success and could have readily treated all types of NPC patients because Lo and Kwong have shown the all type of NPC cells having hypermethylation compared to normal cells and Momparler et al., have used the demethylation agent, 5-aza-2-deoxycytidine to teat squamous cell carcinoma cells. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

Applicant's arguments have been considered but are moot in view of the new ground(s) of rejection above.

### ***Conclusion***

No claims are allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lei Yao, Ph.D. whose telephone number is 571-272-3112. The examiner can normally be reached on 8am-6.00pm Monday-Thursday.

Any inquiry of a general nature, matching or file papers or relating to the status of this application or proceeding should be directed to Kim Downing for Art Unit 1642 whose telephone number is 571-272-0521

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Lei Yao, Ph.D./  
Examiner, Art Unit 1642

/Larry R. Helms/

Supervisory Patent Examiner, Art Unit 1643